Ipilimumab-induced adrenalitis: a possible pitfall in 18F-FDG-PET/CT

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Ipilimumab-Induced Adrenalitis

A Possible Pitfall in ^{18}F-FDG-PET/CT

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Abstract: Ipilimumab is a monoclonal antibody against the inhibitory CTLA-4 receptor expressed on T cells. It provokes an upregulation of the immune system. This substance was approved by the US Food and Drug Administration in 2011 and is since increasingly used as a targeted therapeutic approach for metastasized melanoma. Ipilimumab is known to cause neuroendocrine disorders, such as hypophysitis and adrenal insufficiency. Our case of a 79-year-old patient represents an important imaging pitfall. Imaging findings of newly symmetrically and smoothly enlarged, hypermetabolic adrenal glands in the setting of previous ipilimumab therapy represent drug-induced adrenalitis and not metastatic disease.

Key Words: ipilimimab, monocloncal antibody, malignant melanoma, FDG-PET/CT, adverse effect, adrenalitis, neuroendocrine system

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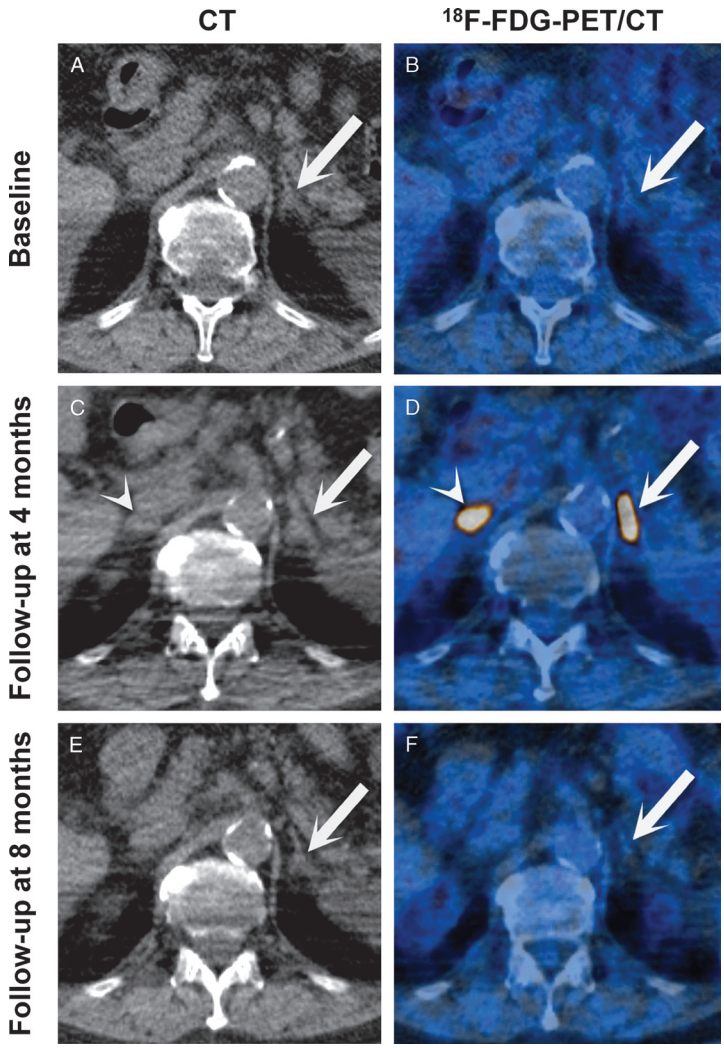

FIGURE 1. ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography (^{18}F-FDG PET/CT) imaging over 8 months in a 79-year-old man with metastasized melanoma. Axial nonenhanced CT image (**A**) and axial ^{18}F-FDG-PET/CT image (**B**) show a normal-sized left adrenal gland with normal FDG uptake (arrow; maximum standardized uptake value (SUV_{max}), 2.4). Adrenocorticotropic hormone (ACTH) and cortisol concentrations were normal. Therapy with ipilimumab was started 1 month later and continued for a total of two months, corresponding to 4 cycles. Four months after the first ^{18}F-FDG-PET/CT was acquired, follow-up CT image (**C**) and ^{18}F-FDG-PET/CT image (**D**) show a smooth thickening of the left adrenal gland with intense FDG uptake (arrow; SUV_{max}, 21.3). The right adrenal gland is seen as well and shows the same imaging features (arrowhead). The lack of nodularity and mass is inconsistent with metastatic disease to the adrenals, which is a major concern in metastasized melanoma. The absence of hyperdensity argues against acute adrenal hemorrhage, which is also known to cause increased FDG uptake, and may occur bilaterally. At this time point, the patient's cortisol level was elevated (579 nmol/L; reference range, 64–327 nmol/L), despite a lack of clinical symptoms. Another 4 months later, shape and metabolic activity of both the left adrenal glands have returned to normal (arrow showing left adrenal gland; SUV_{max}, 2.1; right adrenal partially depicted), as seen on axial nonenhanced CT image (**E**) and axial ^{18}F-FDG-PET/CT image (**F**). There was no evidence of adrenal dysfunction at this time point anymore. Endocrinopathy accounts for 4% to 8% of all adverse effects related to ipilimumab treatment.[1] Ipilimumab is well known for the induction of lymphocytic hypophysitis and anterior panhypopituitarism, which may finally lead to secondary adrenal gland insufficiency in severe cases.[2–5] Other adverse effects include colitis, hepatitis, and reactivation of sarcoid.[6–9] The usual onset of neuroendocrine disorders occurs between 6 and 12 weeks after initializing treatment.[10–12] In our patient, the time interval of 3 months between the start of ipilimumab and the advent of enlarged, hypermetabolic adrenal glands is in line with this period. CT findings of ipilimumab-related autoimmune adrenalitis have hitherto been described in one single case report.[13] Primary adrenal insufficiency is reported as a rare complication in a few clinical studies, probably representing a sequela of previous adrenalitis.[14,15] In conclusion, ^{18}F-FDG-PET/CT findings of symmetrically and smoothly enlarged, hypermetabolic adrenal glands after ipilimumab therapy should raise the suspicion of drug-induced adrenalitis and may imply a monitoring of the patient's adrenal function.